In the Claims

Claims 1-77 (Cancelled)

Claim 78 (New): A composition of matter comprising:

a) an isolated polypeptide selected from the group consisting of:

1) an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112;

2) a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to 1);

3) a functional equivalent of 1) or 2);

4) an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112;

5) the fragment of 2), wherein the fragment comprises the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

6) the fragment of 2), wherein the fragment consists of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

7) the fragment of 2), wherein the fragment comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

8) the fragment of 2), wherein the fragment consists of an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

9) the functional equivalent of 3), wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor;

10) the functional equivalent of 9), wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80% sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof;

11) the functional equivalent of 3), wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112;

12) the fragment of 2), wherein the fragment has an antigenic determinant in common with the amino acid sequence of 1), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112;

b) a purified nucleic acid molecule:

1) encoding a polypeptide of any of a1) to a12);

2) comprising the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof;

3) consisting of the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof;

4) comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing;

5) consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing;

6) that hybridizes under high stringency conditions with a nucleic acid molecule of any of b1) to b5);

c) a vector comprising a nucleic acid molecule according to any one of b1) to b6);

d) a host cell transformed with a vector or a nucleic acid molecule according to any one of b) or c);

e) a ligand:

1) that binds specifically to the polypeptide of any of a1) to a12);

2) which is an antibody that binds specifically to the polypeptide of any of a1) to a12);

f) a compound:

1) that increases the level of expression or activity of a polypeptide according to any of a1) to a12);

2) that decreases the level of expression or activity of a polypeptide according to any of a1) to a12);

g) a compound that binds to a polypeptide according to any of a1) to a12) without inducing any of the biological effects of the polypeptide;

h) a compound that binds to a polypeptide according to any of a1) to a12) without inducing any of the biological effects of the polypeptide, wherein the compound is a natural or modified substrate, ligand, enzyme, receptor or structural or functional mimetic;

i) a pharmaceutical composition comprising any one of a) to h), and a pharmaceutically acceptable carrier;

j) a vaccine composition comprising any one of a1) to a12) or b1) to b6);

k) a kit for diagnosing disease, comprising a first container containing a nucleic acid probe that hybridizes under stringent conditions with a nucleic acid molecule of any one of b1) to b6), a second container containing primers useful for amplifying the nucleic acid molecule, and instructions for using the probe and primers for facilitating the diagnosis of disease;

l) a kit for diagnosing disease, comprising a first container containing a nucleic acid probe that hybridizes under stringent conditions with a nucleic acid molecule of any one of b1) to b6); a second container containing primers useful for amplifying the nucleic acid molecule; a third container holding an agent for digesting unhybridized RNA; and instructions for using the probe and primers for facilitating the diagnosis of disease.

m) a kit comprising an array of nucleic acid molecules, at least one of which is a nucleic acid molecule according to any one of b1) to b6);

n) a kit comprising one or more antibodies that bind to a polypeptide as recited in any one of a1) to a12); and a reagent useful for the detection of a binding reaction between the one or more antibodies and the polypeptide; or

o) a transgenic or knockout non-human animal that has been transformed to express higher, lower, or absent levels of a polypeptide according to any one of a1) to a12).

Claim 79 (New): A method of using a composition of matter, comprising obtaining a composition of matter according to claim 78 and using said composition of matter in a method selected from: diagnosing a disease in a patient treatment of a disease in a patient; monitoring the therapeutic treatment of a disease; identification of a compound that is effective in the treatment and/or diagnosis of a disease; and screening candidate compounds.

Claim 80 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for treatment of a disease, comprising administering to the patient a polypeptide selected from the group consisting of:

a) an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112;

b) a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to a);

c) a functional equivalent of a) or b);

d) an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112;

e) the fragment of b), wherein the fragment comprises the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

f) the fragment of b), wherein the fragment consists of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

g) the fragment of b), wherein the fragment comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

h) the fragment of b), wherein the fragment consists of an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

i) the functional equivalent of c), wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor;

j) the functional equivalent of c), wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80% sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof;

k) the functional equivalent of c), wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and

l) the fragment of b), wherein the fragment has an antigenic determinant in common with the amino acid sequence of a), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112.

Claim 81 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for treatment of a disease, comprising administering to the patient a nucleic acid molecule:

a) encoding a polypeptide selected from the group consisting of: an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112; a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with the polypeptide; a functional equivalent of the amino acid sequence or the fragment; an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112; a fragment comprising the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof; a fragment consisting of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof; a fragment comprising an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID

NO:121, or a functional equivalent of any of the foregoing; a fragment consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing; a functional equivalent of SEQ ID NO:68 or SEQ ID NO:112, wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor; a functional equivalent of SEQ ID NO:68 or SEQ ID NO:112, wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80% sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof; a functional equivalent SEQ ID NO:68 or SEQ ID NO:112, wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and a fragment of SEQ ID NO:68 or SEQ ID NO:112, wherein the fragment has an antigenic determinant in common with the amino acid sequence of 1), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112;

b) comprising the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof;

c) consisting of the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof;

d) comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing;

e) consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

f) that hybridizes under high stringency conditions with a nucleic acid molecule of any of a) to e).

Claim 82 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for treatment of a disease, comprising administering to the patient a vector comprising a nucleic acid molecule:

a) encoding a polypeptide selected from the group consisting of:

1) an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112;

2) a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to 1);

3) a functional equivalent of 1) or 2);

4) an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112;

5) the fragment of 2), wherein the fragment comprises the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

6) the fragment of 2), wherein the fragment consists of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

7) the fragment of 2), wherein the fragment comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

8) the fragment of 2), wherein the fragment consists of an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

9) the functional equivalent of 3), wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor;

10) the functional equivalent of 3), wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80% sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof;

11) the functional equivalent of 3), wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and

12) the fragment of 2), wherein the fragment has an antigenic determinant in common with the amino acid sequence of 1), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; or

b) comprising the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

c) consisting of the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

d) comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

e) consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

f) that hybridizes under high stringency conditions with a nucleic acid molecule of any of a) to e).

Claim 83 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for treatment of a disease, comprising administering to the patient a host cell transformed with a vector or a nucleic acid molecule:

a) encoding a polypeptide selected from the group consisting of:

1) an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112;

2) a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to 1);

3) a functional equivalent of 1) or 2);

4) an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112;

5) the fragment of 2), wherein the fragment comprises the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

6) the fragment of 2), wherein the fragment consists of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

7) the fragment of 2), wherein the fragment comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

8) the fragment of 2), wherein the fragment consists of an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

9) the functional equivalent of 3). wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor;

10) the functional equivalent of 3), wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80% sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof;

11) the functional equivalent of 3), wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and

12) the fragment of 2), wherein the fragment has an antigenic determinant in common with the amino acid sequence of 1), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; or

b) comprising the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

c) consisting of the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

d) comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

e) consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

f) that hybridizes under high stringency conditions with a nucleic acid molecule of any of a) to e).

Claim 84 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for treatment of a disease, comprising administering to the patient a ligand that binds specifically to a polypeptide, or which is an antibody that binds specifically to the polypeptide, and wherein the polypeptide is selected from the group consisting of:

a) an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112;

b) a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to a);

c) a functional equivalent of a) or b);

d) an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112;

e) the fragment of b), wherein the fragment comprises the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

f) the fragment of b), wherein the fragment consists of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

g) the fragment of b), wherein the fragment comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

h) the fragment of b), wherein the fragment consists of an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

i) the functional equivalent of c) wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor;

j) the functional equivalent of c), wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80% sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof;

k) the functional equivalent of c), wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and

l) the fragment of b), wherein the fragment has an antigenic determinant in common with the amino acid sequence of a), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112.

Claim 85 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for treatment of a disease, comprising administering to the patient a compound:

a) that increases the level of expression or activity of a polypeptide comprising:

1) an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112; or

2) a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to 1); or

3) a functional equivalent of 1) or 2); or

4) an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112; or

5) the fragment of 2), wherein the fragment comprises the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof; or

6) the fragment of 2), wherein the fragment consists of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof; or

7) the fragment of 2), wherein the fragment comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing; or

8) the fragment of 2), wherein the fragment consists of an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing; or

9) the functional equivalent of 3), wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor; or

10) the functional equivalent of 3), wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80% sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof; or

11) the functional equivalent of 3), wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; or

12) the fragment of 2), wherein the fragment has an antigenic determinant in common with the amino acid sequence of 1), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; or

b) that decreases the level of expression or activity of a polypeptide according to any of a1) to a12); or

c) that binds to a polypeptide according to any of a1) to a12) without inducing any of the biological effects of the polypeptide; or

d) that binds to a polypeptide according to any of a1) to a12) without inducing any of the biological effects of the polypeptide, wherein the compound is a natural or modified substrate, ligand, enzyme, receptor or structural or functional mimetic.

Claim 86 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for treatment of a disease, comprising administering to the patient a pharmaceutical composition comprising a pharmaceutically acceptable carrier and any one of a) to h):

a) an isolated polypeptide selected from the group consisting of:

1) an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112;

2) a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to 1);

3) a functional equivalent of 1) or 2);

4) an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112;

5) the fragment of 2), wherein the fragment comprises the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

6) the fragment of 2), wherein the fragment consists of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

7) the fragment of 2), wherein the fragment comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

8) the fragment of 2), wherein the fragment consists of an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

9) the functional equivalent of 3), wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor;

10) the functional equivalent of 3), wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80% sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof;

11) the functional equivalent of 3), wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and

12) the fragment of 2), wherein the fragment has an antigenic determinant in common with the amino acid sequence of 1), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112;

b) a purified nucleic acid molecule:

1) encoding a polypeptide of any of a1) to a12);

2) comprising the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof;

3) consisting of the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof;

4) comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing;

5) consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing;

6) that hybridizes under high stringency conditions with a nucleic acid molecule of any of b1) to b5);

c) a vector comprising a nucleic acid molecule according to any one of b1) to b6);

d) a host cell transformed with a vector or a nucleic acid molecule according to any one of b) or c);

e) a ligand:

1) that binds specifically to the polypeptide of any of a1) to a12);

2) which is an antibody that binds specifically to the polypeptide of any of a1) to a12);

f) a compound:

1) that increases the level of expression or activity of a polypeptide according to any of a1) to a12);

2) that decreases the level of expression or activity of a polypeptide according to any of a1) to a12);

g) a compound that binds to a polypeptide according to any of a1) to a12) without inducing any of the biological effects of the polypeptide;

h) a compound that binds to a polypeptide according to any of a1) to a12) without inducing any of the biological effects of the polypeptide, wherein the compound is a natural or modified substrate, ligand, enzyme, receptor or structural or functional mimetic.

Claim 87 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for treatment of a disease, and wherein the disease includes reproductive disorders, cell proliferative disorders, including neoplasm, melanoma, lung, colorectal, breast, pancreas, head and neck and other solid tumours; myeloproliferative disorders, such as leukemia, non-Hodgkin lymphoma, leukopenia, thrombocytopenia, angiogenesis disorder, Kaposis' sarcoma; autoimmune/inflammatory disorders, including allergy, inflammatory bowel disease, pancreatitis, arthritis, psoriasis, psoriasis vulgaris, respiratory tract inflammation, asthma, and organ transplant rejection; cardiovascular disorders, including hypertension, oedema, angina, atherosclerosis, thrombosis, sepsis, shock, reperfusion injury, and ischemia, particularly ischemic heart disease; neurological disorders including central nervous system disease, Alzheimer's disease, brain injury, Parkinson's disease, amyotrophic lateral sclerosis, and pain; developmental disorders; metabolic disorders including diabetes mellitus osteoporosis, and obesity, AIDS, renal disease,

particularly idiopathic nephrotic syndrome; lung injury; infections including viral infection, bacterial infection, fungal infection and parasitic infection, particularly *Trypanosoma cruzi* infection and other pathological conditions.

Claim 88 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for treatment of a disease, and wherein the disease is one for which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an agonist.

Claim 89 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for treatment of a disease, and wherein the disease is one for which expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an antagonist.

Claim 90 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide, or assessing the activity of the polypeptide, in tissue from said patient; and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease, and wherein the polypeptide is selected from the group consisting of:

a) an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112;

b) a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to a);

c) a functional equivalent of a) or b);

d) an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112;

e) the fragment of b), wherein the fragment comprises the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

f) the fragment of b), wherein the fragment consists of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

g) the fragment of b), wherein the fragment comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

h) the fragment of b), wherein the fragment consists of an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

i) the functional equivalent of c), wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor;

j) the functional equivalent of c), wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80% sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof;

k) the functional equivalent of c), wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and

l) the fragment of b), wherein the fragment has an antigenic determinant in common with the amino acid sequence of a), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112.

Claim 91 (New): The method of claim 90, which is carried out *in vitro*.

Claim 92 (New): The method of claim 90, comprising the steps of:

a) contacting a ligand with a biological sample under conditions suitable for the formation of a ligand-polypeptide complex; and

b) detecting said complex, wherein the ligand binds specifically to the polypeptide of any of a) to l) of claim 90, or wherein the ligand is an antibody that binds specifically to the polypeptide of any of a) to l) of claim 90.

Claim 93 (New): The method of claim 90, comprising the steps of:

a) contacting a sample of tissue from the patient with a nucleic acid probe under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule and the probe;

b) contacting a control sample with said probe under the same conditions used in step a); and

c) detecting the presence of hybrid complexes in said samples; wherein detection of levels of the hybrid complex in the patient sample that differ from levels of the hybrid complex in the control sample is indicative of disease, wherein the nucleic acid molecule:

1) encodes a polypeptide of any of a) to l) of claim 90; or

2) comprises the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

3) consists of the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

4) comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

5) consists of a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

6) hybridizes under high stringency conditions with a nucleic acid molecule of any of c1) to c5).

Claim 94 (New): The method of claim 90, comprising the steps of:

a) contacting a sample of nucleic acid from tissue of the patient with a nucleic acid primer under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule and the primer;

b) contacting a control sample with said primer under the same conditions used in step a); and

c) amplifying the sampled nucleic acid; and

d) detecting the level of amplified nucleic acid from both patient and control samples; wherein detection of levels of the amplified nucleic acid in the patient sample that differ significantly from levels of the amplified nucleic acid in the control sample is indicative of disease; and wherein the nucleic acid molecule:

1) encodes a polypeptide of any of a) to l) of claim 90; or

2) comprises the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

3) consists of the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

4) comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

5) consists of a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

6) hybridizes under high stringency conditions with a nucleic acid molecule of any of d1) to d5).

Claim 95 (New): The method of claim 90, comprising:

a) obtaining a tissue sample from a patient being tested for disease;

b) isolating a nucleic acid molecule from said tissue sample; and

c) diagnosing the patient for disease by detecting the presence of a mutation which is associated with disease in the nucleic acid molecule as an indication of the disease, wherein the nucleic acid molecule:

1) encodes a polypeptide of any of a) to l) of claim 90; or

2) comprises the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

3) consists of the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

4) comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

5) consists of a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

6) hybridizes under high stringency conditions with a nucleic acid molecule of any of c1) to c5).

Claim 96 (New): The method of claim 95, further comprising amplifying the nucleic acid molecule to form an amplified product and detecting the presence or absence of a mutation in the amplified product.

Claim 97 (New): The method of claim 95, wherein the presence or absence of the mutation in the patient is detected by contacting said nucleic acid molecule with a nucleic acid probe that hybridizes to said nucleic acid molecule under stringent conditions to form a hybrid double-stranded molecule, the hybrid double-stranded molecule having an unhybridized portion of the nucleic acid probe strand at any portion corresponding to a mutation associated with disease; and detecting the presence or absence of an unhybridized portion of the probe strand as an indication of the presence or absence of a disease-associated mutation.

Claim 98 (New): The method of claim 96, wherein said disease includes, but is not limited to reproductive disorders, cell proliferative disorders, including neoplasm, melanoma, lung, colorectal, breast, pancreas, head and neck and other solid tumours; myeloproliferative disorders, such as leukemia, non-Hodgkin lymphoma, leukopenia, thrombocytopenia, angiogenesis disorder, Kaposis' sarcoma; autoimmune/inflammatory disorders, including allergy, inflammatory bowel disease, pancreatitis, arthritis, psoriasis, psoriasis vulgaris, respiratory tract inflammation, asthma, and organ transplant rejection; cardiovascular disorders, including hypertension, oedema, angina, atherosclerosis, thrombosis, sepsis, shock, reperfusion injury, and ischemia, particularly ischemic heart disease; neurological disorders including central nervous system disease, Alzheimer's disease, brain injury, Parkinson's disease, amyotrophic lateral sclerosis, and pain; developmental disorders; metabolic disorders including diabetes mellitus, osteoporosis, and obesity, AIDS, renal disease, particularly idiopathic nephrotic syndrome; lung injury; infections including viral infection, bacterial infection, fungal infection and parasitic infection particularly *Trypanosoma cruzi* infection and other pathological conditions.

Claim 99 (New): The method of claim 96, wherein said disease is a disease in which alpha-2-macroglobulin-like proteinase inhibitors are implicated.

Claim 100 (New): The method of claim 99, wherein said method of using a composition of matter comprises the method of monitoring the therapeutic treatment of a disease, comprising monitoring over a period of time the level of expression or activity of a polypeptide, or the level of expression of a nucleic acid molecule in tissue from said patient, wherein altering said level of expression or activity over the period of time towards a control level is indicative of regression of said disease, wherein the polypeptide is selected from the group consisting of:

a) an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112;

b) a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to a);

c) a functional equivalent of a) or b);

d) an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112;

c) the fragment of b), wherein the fragment comprises the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

f) the fragment of b), wherein the fragment consists of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

g) the fragment of b), wherein the fragment comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

h) the fragment of b), wherein the fragment consists of an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

i) the functional equivalent of c), wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor;

j) the functional equivalent of c), wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80% sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof;

k) the functional equivalent of c), wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and

l) the fragment of b), wherein the fragment has an antigenic determinant in common with the amino acid sequence of a), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and

wherein the nucleic acid molecule:

m) comprises a nucleic acid sequence encoding the polypeptide of any of a) to l); or

n) comprises the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

o) consists of the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

p) comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

q) consists of a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

r) that hybridizes under high stringency conditions with a nucleic acid molecule of any of m) to q).

Claim 101 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for identification of a compound that is effective in the treatment and/or diagnosis of a disease, comprising contacting a polypeptide or a nucleic acid molecule with one or more compounds suspected of possessing binding affinity for said polypeptide or nucleic acid molecule, and selecting a compound that binds specifically to said nucleic acid molecule or polypeptide, wherein the polypeptide is selected from the group consisting of:

a) an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112;

b) a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to a);

c) a functional equivalent of a) or b);

d) an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112;

e) the fragment of b), wherein the fragment comprises the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

f) the fragment of b), wherein the fragment consists of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

g) the fragment of b), wherein the fragment comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

h) the fragment of b), wherein the fragment consists of an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

i) the functional equivalent of c), wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor;

j) the functional equivalent of c), wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80% sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof;

k) the functional equivalent of c), wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and

l) the fragment of b), wherein the fragment has an antigenic determinant in common with the amino acid sequence of a), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and

wherein the nucleic acid molecule:

m) comprises a nucleic acid sequence encoding the polypeptide of any of a) to l); or

n) comprises the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

o) consists of the nucleic acid sequence recited in SEQ ID NO:67 or SEQ ID NO:111, or a redundant equivalent or fragment thereof; or

p) comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

q) consists of a nucleic acid sequence selected from the group consisting of SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, and SEQ ID NO:122, or a redundant equivalent of any of the foregoing; or

r) that hybridizes under high stringency conditions with a nucleic acid molecule of any of m) to q).

Claim 102 (New): The method of claim 79, wherein said method of using a composition of matter comprises the method for screening candidate compounds, comprising contacting a non-human transgenic or knockout animal with a candidate compound and determining the effect of the compound on the disease of the animal, wherein the animal has been transformed to express higher, lower, or absent levels of a polypeptide selected from the group consisting of:

a) an amino acid sequence comprising that recited in SEQ ID NO:68 or SEQ ID NO:112;

b) a fragment of said amino acid sequence which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to a);

c) a functional equivalent of a) or b);

d) an amino acid sequence consisting of that recited in SEQ ID NO:68 or SEQ ID NO:112;

e) the fragment of b), wherein the fragment comprises the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

f) the fragment of b), wherein the fragment consists of the amino acid sequence of SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof;

g) the fragment of b), wherein the fragment comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

h) the fragment of b), wherein the fragment consists of an amino acid sequence selected from the group consisting of: SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent of any of the foregoing;

i) the functional equivalent of c), wherein the functional equivalent is homologous to the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, and wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor;

j) the functional equivalent of c), wherein the functional equivalent is an alpha-2-macroglobulin-like proteinase inhibitor, and wherein the functional equivalent has greater than 80%

sequence identity with the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112, or with an active fragment thereof;

k) the functional equivalent of c), wherein the functional equivalent exhibits significant structural homology with a polypeptide comprising the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112; and

l) the fragment of b), wherein the fragment has an antigenic determinant in common with the amino acid sequence of a), and wherein the antigenic determinant consists of at least 7 amino acid residues from the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112.

Claim 103 (New): An isolated polypeptide comprising:

a) the amino acid sequence recited in SEQ ID NO:68 or SEQ ID NO:112;

b) a fragment thereof which functions as an alpha-2-macroglobulin-like proteinase inhibitor, or has an antigenic determinant in common with a polypeptide according to a); or

c) a functional equivalent of a) or b).

Claim 104 (New): The isolated polypeptide of claim 103, wherein the polypeptide is a fragment comprising the amino acid sequence recited in SEQ ID NO:113 or SEQ ID NO:115, or a functional equivalent thereof.

Claim 105 (New): The isolated polypeptide of claim 103, wherein the polypeptide is a fragment comprising an amino acid sequence selected from the group consisting of SEQ ID NO:117, SEQ ID NO:119, and SEQ ID NO:121, or a functional equivalent thereof.